

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 10 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

### REMARKS

Claims 12, 18-21, 29, 35-39, and 43-44 are pending after the entry of this amendment. New claim 44 is added herein. Claims 12 and 38 are amended. Claim 12 is amended to more clearly recite the claimed subject matter. Claim 38 is amended to remove negative limitation from the claim. Basis for the amendment can be found in claim 38 as originally filed.

### **REJECTION OF CLAIMS 12, 18-21, 29, 35-39 AND 43 UNDER 35 U.S.C. §102(b)/103(a)**

Claims 12, 18-21, 29, 35-39, and 43 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 4,421,767 to Palfreyman *et al* ("Palfreyman"). The Office Action alleges that Palfreyman discloses collections of compounds (reading on the claimed 'combinatorial library') that read directly on the instant formulas 1 and 23. It is alleged that the compounds of the reference read on the instant claims where the compounds are of formula 23, wherein  $R^1$  and  $R^2 = H$ ;  $R^3 = H$ ;  $R^9 = \text{aryl}$ ; and  $R^{10}$  and  $R^{11} = \text{fluoro, chloro or bromo}$ . Pointing to particular molecular formulae disclosed in Palfreyman, the Office Action alleges that "the collections of compounds of the reference reads on applicant's definition of 'combinatorial library' (see, instant specification, page 7, lines 14-36)." The Office Action further alleges that the collection of compounds of Palfreyman meet all of the limitations of the claimed library except for the product by process limitations and would allegedly either anticipate or render obvious the claimed library. The rejection is respectfully traversed.

### **ANALYSIS**

#### **1. Anticipation Analysis**

##### **Relevant law**

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir. 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundsciber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, *adopted* 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention".

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 11 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

*In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover it is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference *Lindemann Maschinen-fabrik GmbH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

#### **Instant claims**

Claim 12 is directed to a combinatorial library of a plurality of compounds, wherein the plurality of compounds in the combinatorial library are prepared by a process described therein.

Claims 18-21, 29, 35-39 and 43-44 depend from claim 12 and further define the library of claim 12.

#### **Disclosure of Palfreyman et al.**

Palfreyman discloses individual chemical compounds represented by formula I, II or III for use in treating depression. The reference further describes the preparation of some of the individual compounds disclosed therein. The reference does not disclose a combinatorial library, as defined in the instant application.

#### **Differences between the instant claims and the disclosure of the reference**

Instant claim 12 is directed to a combinatorial library of a plurality of compounds wherein the plurality of compounds is prepared by a process described therein. Therefore the claim encompasses a collection of compounds. The cited reference does not disclose a collection of compounds as instantly claimed. The reference discloses individual compounds represented as a Markush group. The Office Action is mischaracterizing a Markush group representation of individual compounds in the reference as a library of compounds. A description of a Markush group of individual compounds is a representation of individual compounds in the alternative and is not the same as a collection of compounds. The instant claims are clearly directed to a collection of compounds that results from the process recited therein. There is no disclosure of

Applicant : Nicos A. Petasis and Iia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 12 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

"a collection of compounds" in the cited reference nor is there any disclosure of a method to prepare such a collection of compounds.

Applicant respectfully submits that the specification on page 7, lines 14-16 recites:

The term "combinatorial library" as used herein refers to a set of compounds that are made by the same process, by varying one or more of the reagents.

Further, the instant specification describes that libraries are prepared as a "mixture of compounds", in which individual compounds can be identified and distinguished by physical and/or chemical characteristics (see specification page 7, lines 16-22). The instant specification also describes that libraries are prepared as collections of individual compounds identified by their respective positions in an array, which are prepared by massively parallel synthesis of collections of individual compounds (see page 7, lines 22-25). The instant specification further describes that libraries are prepared as "a set of sub-pools, each having a known element and a random element", in which collections of individual compounds are identified by deconvolution (see page 7, lines 25-36). Thus, in each case, the compounds in the library are related by location -whether as members of a common mixture, individual compounds distributed in a common array, or as members distributed in sub-pools- and by preparation, according to the methods described in the specification.

By contrast, the cited reference is directed to individual compounds and methods of their use. The individual compounds in the reference are disclosed as formula I, II or III. The reference does not disclose a collection of compounds as claimed in instant claim 12. Therefore, Palfreyman does not anticipate claim 12. Since all pending claims are dependent on claim 12, it does not anticipate any of the pending claims.

## 2. Non-Obviousness analysis

### Relevant Law

[I]n order to establish a *prima facie* case of obviousness, there must be evidence, preferably a teaching, suggestion, incentive or inference from the cited art or in the form of generally available knowledge that one of ordinary skill would have been led to modify the relevant teaching to arrive at what is claimed. *In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43,

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 13 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

51 (CCPA 1963).

The prior art must provide a motivation whereby one of ordinary skill in the art would have been led to do that which the applicant has done. *Stratosflex Inc. v Aeroquip Corp.*, 713 F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir. 1983

#### Claims

The claims are summarized above.

#### Analysis

Palfreyman does not provide any teaching or suggestion that would have lead one of ordinary skill in the art to do that which applicant has done. There is no suggestion in Palfreyman of a combinatorial library of compounds as claimed in the instant claims. The reference does not teach or suggest a method to prepare a collection of compounds as instantly claimed. Neither does it teach or suggest modification of the method disclosed therein to arrive at the instant library of compounds. The reference suggests individual compounds represented in a Markush group format. A person of ordinary skill in the art would not be able to arrive at the instantly claimed library of compounds based on the teachings of Markush structures in the reference.

The combinatorial library of the instant claims would further not have been obvious to one of skill in the art based on the teachings of Palfreyman because the method of using a combinatorial library is different than that of using individual compounds taught in the reference. For example, a combinatorial library has a use in methods of screening the compounds in the library against various targets whereas the individual compounds taught in the reference have use in testing for a particular target. Therefore, based on the teaching of individual compounds in the reference, which are used in treating depression, one of ordinary skill in the art would not have arrived at the instant combinatorial library of compounds that has a use for screening against various targets.

As discussed above, claim 12 and all claims dependent thereon, are directed to a combinatorial library of compounds. There is no teaching or suggestion in Palfreyman of a library of compounds as instantly claimed.

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 14 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

### Rebuttal to Examiner's Arguments

The Office action alleges that although Palfreyman does not disclose that their collection of compounds (i.e. libraries) are made by the same process, the products of Palfreyman would appear to be the same as those recited by the instant claims.

Applicant respectfully submits that Palfreyman discloses individual compounds represented by formula I, II or III. The disclosure of the reference is a representation of individual compounds in a Markush group format. As discussed above, the instant claims are directed to a combinatorial library or a collection of compounds. A collection of compounds is not the same as individual compounds in the collection. There is no disclosure of a combinatorial library of compounds in the reference.

The Office Action further alleges that any collection of compounds meeting the structural requirements of the instant claims reads on the claimed library.

Applicant directs Examiner's attention to the fact that the reference does not disclose a collection of compounds. It merely discloses individual compounds of formula I, II or III represented in a Markush format. Therefore, the disclosure of the cited reference does not read on the instantly claimed combinatorial library of a plurality of compounds wherein the plurality of compounds is prepared by a process described therein.

### RESPONSE TO ADVISORY ACTION

**Combinatorial libraries are not necessarily composed of mixtures of compounds, but can be a collection of individual, pure compounds**

The Advisory Action alleges that Palfreyman *et al.* anticipates the claimed library because the specification discloses that the combinatorial libraries are not necessarily composed of mixtures of compounds, but can be a set of individual, pure compounds.

Applicant respectfully submits that the combinatorial library of the instant claims encompasses **mixtures of compounds and a collection of individual, pure compounds** prepared by the process recited in the claim. The claim is **not directed to individual compounds**. By contrast, the cited reference discloses individual compounds of formula I, formula II and formula III, and methods of their use. The reference does not disclose a

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 15 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

collection of compounds prepared by the process recited in the claim as claimed in instant claim 12. Therefore, Palfreyman does not anticipate claim 12.

**Features not recited in the claim**

The Advisory Action states that the applicant argues that the reference fails to show certain features of the claimed combinatorial library. The Advisory Action urges that the features, compounds in a library are related by location and by preparation, upon which applicant relies are not recited in the claim.

Applicant respectfully submits that the instant claim recites the feature that the plurality of compounds in the combinatorial library are prepared by the process recited in the claim. The library can be made as a mixture of compounds, or as a collection of individual pure compounds, depending on the methods used for identification of active compounds. When the library is made as a mixture of compounds, the compounds in the library are related by location as members of a common mixture having unique chemical and/or physical characteristics. When the library is made as a collection of individual pure compounds, the compounds are related by location as individual compounds distributed in a common array. The instant claims are contemplated to encompass any combinatorial library of a plurality of compounds wherein the plurality of compounds in the combinatorial library are prepared by the process recited in the claim. The individual members are related by location based on whether the library is prepared as a mixture of compounds or as a collection of individual pure compounds. Therefore, there is no need to recite this feature in the claim.

**Plurality of compounds**

The Advisory Action alleges that claim 1 is drawn to a plurality of compounds, where one or more of the plurality of compounds in the combinatorial library are prepared by the claimed process. The Advisory Action urges that Palfreyman *et al.* teaches the compounds of Formula I, II or III may be used in combination with aromatic-L-amino acid decarboxylase (AADC). It is alleged that the reference further anticipates claim 1, in teaching a plurality of compounds (AADC plus compound of Formula I, II or III), where one of the plurality of compounds is prepared by the claimed process.

Applicant : Nicos A. Petasis and Ilia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 16 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

First, applicant notes that the claim at issue is claim 12. Claim 1 had been cancelled from the instant case in a previous amendment. Second, applicant respectfully submits that the amended claim 12 does not recite the limitation that one or more of the plurality of compounds in the combinatorial library are prepared by the claimed process. The limitation in the amended claim recites that the plurality of compounds in the combinatorial library are prepared by the process recited in the claim. Therefore, the plurality of compounds in the cited reference (AADC plus compound of Formula I, II or III), where one of the plurality of compounds is prepared by the claimed process, does not anticipate the instant claim.

**REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

Claim 38 has been rejected under 35 U.S.C. first paragraph as containing matter which was not described in the specification in such a way as to indicate that inventors had possession of the claimed invention. Specifically, the Office Action has objected to the negative limitation "provided that R<sup>10</sup> and R<sup>11</sup> are not both hydrogen."

Claim 38 has been amended to remove the negative limitation and is believed to be in condition for allowance. Applicants respectfully request reconsideration and withdrawal of this rejection

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Applicant : Nicos A. Petasis and Iia A. Zavialov  
Serial No. : 09/699,076  
Filed : October 27, 2000  
Page : 17 of 17

Attorney's Docket No.: 06666-005002 / USC 2616

In view of the above amendments and remarks, reconsideration and allowance of the application is respectfully requested.

Applicant hereby petitions under 37 C.F.R. §1.136 for two (2) months extension of time. The Commissioner is hereby authorized to charge \$385.00 for the filing Request for Continued Examination and \$210.00 for 2 month extension of time, apply any other charges, or any credits, to Deposit Account 06-1050.

Respectfully submitted,

Date:

9/8/04



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